

## Supporting Information

# A High Yielding Preparation of $\beta$ -Ketonitriles

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**General Information.** Unless otherwise noted, all reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring. Tetrahydrofuran and dichloromethane, were filtered through a column of activated alumina under an atmosphere of argon. Benzene (A.C.S. reagent grade), and acetone (Optima grade) were purchased from Fisher and used without further purification. Ethyl alcohol, USP grade, was purchased from Pharmco and used without further purification. Benzoyl isocyanate (95%) was purchased from Alfa and used without further purification. Purification of reaction products was carried out by column chromatography using EM Reagents silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 250  $\mu\text{m}$  silica gel 60-F<sub>254</sub> plates. Visualization was accomplished with UV light and aqueous ceric ammonium molybdate solution or anisaldehyde followed by heating.

Melting points were measured with a Thomas Hoover Capillary Melting Point Apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer.

<sup>1</sup>H NMR spectra were recorded on Bruker Avance 300 (300 MHz) or Avance 400 (400 MHz) spectrometers and are reported in ppm using solvent as the internal standard (CDCl<sub>3</sub> at 7.26 ppm, (CD<sub>3</sub>)<sub>2</sub>CO at 2.05 ppm, (CD<sub>3</sub>)<sub>2</sub>SO at 2.50 ppm). Data are reported as: (b = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constant(s) in Hz, integration). <sup>13</sup>C NMR spectra were recorded on Avance 300 (75 MHz) or Avance 400 (100 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane, with the solvent resonance employed as the internal standard (CDCl<sub>3</sub> at 77.1 ppm, (CD<sub>3</sub>)<sub>2</sub>CO at 29.8 ppm, (CD<sub>3</sub>)<sub>2</sub>SO at 39.5 ppm). High resolution mass spectra were obtained on Jeol HMS 600-H spectrometers in the Brown University Mass Spectrometry Laboratory. Exact mass measurements were obtained by internal calibration with an appropriate lock mass compound.

## General procedure A.

**3-Oxo-2-phenyl-pentanenitrile (6bw).** Potassium *tert*-pentylate (1.33 ml, 2.61 mmol) was added dropwise to a solution of phenylacetone nitrile (**4b**, 101.5 mg, 0.87 mmol) in anhydrous THF (3 ml) followed by ethyl propionate (0.32 ml, 3.48 mmol). The mixture was stirred at R.T. for 20 minutes, then diluted with 1N HCl solution (25 ml), H<sub>2</sub>O (75 ml) and ethyl acetate (100 ml). The organic layer was separated, washed with H<sub>2</sub>O (50 ml  $\times$  2) and brine (50 ml  $\times$  2), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated to afford a light yellow oil. Column chromatography (SiO<sub>2</sub>, 20% EtOAc/hexanes) provided 149.3 mg (99%) of **6bw** as a colorless oil:  $R_f$  = 0.26 (25% EtOAc/hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>)  $\delta$  7.49-7.38 (m, 5H), 4.70 (s, 1H), 2.78-2.53 (m, 2H), 1.06 (t,  $J$  = 7.2 Hz, 3H); <sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>)  $\delta$  199.9, 130.3, 130.0, 129.6, 128.3, 116.8, 51.1, 33.5, 8.0; IR (film) 2999, 2980, 2941, 2249, 1728, 1494, 1456, 1403, 1384, 1350, 1286, 1199, 1174, 1102 cm<sup>-1</sup>; HRMS (FAB-MS)  $m/z$  196.0735 (196.0738 calc. for C<sub>11</sub>H<sub>11</sub>N<sub>1</sub>O<sub>1</sub>Na, M+Na<sup>+</sup>).

**3-Oxo-2, 3-diphenyl-propionitrile (6bx).** Using general procedure A, phenylacetone nitrile (**4b**, 101.5 mg, 0.87mmol) was converted into 191.7 mg (99%) of **6bx** as a colorless oil following column chromatography (SiO<sub>2</sub>, 25% EtOAc/Hexanes):  $R_f$  = 0.23 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>)  $\delta$  7.98-7.95 (m, 2H), 7.64-7.59 (m, 1H), 7.51-7.37 (m, 7H), 5.62 (s, 1H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>)  $\delta$  189.3, 134.9, 133.9, 130.7, 130.1, 129.7, 129.6, 129.4, 128.7, 116.9, 47.1; IR (film) 3064, 2251, 2209, 1691, 1596, 1494, 1450, 1393, 1324, 1299, 1230 cm<sup>-1</sup>; HRMS (FAB)  $m/z$  244.0738 (244.0738 calc. for C<sub>15</sub>H<sub>11</sub>N<sub>1</sub>O<sub>1</sub>Na, M+Na<sup>+</sup>).

**4-Methyl-3-oxo-2-phenyl-pentanenitrile (6by).** Using general procedure A, phenylacetone nitrile (**4b**, 185  $\mu$ L, 1.60 mmol) was converted into 294.8 mg (98.4%) of **6by** as a colorless oil following column chromatography (SiO<sub>2</sub>, 25% EtOAc/Hexanes):  $R_f$  = 0.40 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>)  $\delta$  7.48-7.39 (m, 5H), 4.82 (s, 1H), 2.98-2.89 (m, 1H), 1.10 (dd,  $J$  = 7.0 Hz, 6.8 Hz, 6H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>)  $\delta$  203.2, 130.3, 129.9, 129.6, 129.1, 128.5, 116.0, 49.6, 38.9, 19.9, 19.3, 18.9; IR (film) 2976, 2250, 2205, 1726, 1456 cm<sup>-1</sup>; HRMS (FAB-MS)  $m/z$  210.0898 (210.0895 calc. for C<sub>12</sub>H<sub>13</sub>N<sub>1</sub>O<sub>1</sub>Na, M+Na<sup>+</sup>).

**4-Cyclohexyl-3-oxo-2-phenyl-butyronitrile (6bz).** Using general procedure A, phenylacetone nitrile (**4b**, 159  $\mu$ L, 1.38 mmol) was converted into 323.1 mg (99.5%) of **6bz** as a colorless oil following column chromatography (SiO<sub>2</sub>, 25% EtOAc/Hexanes):  $R_f$  = 0.32 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>)  $\delta$  7.51-7.26 (m, 5H), 4.67 (s, 1H), 2.56-2.26 (m, 2H), 1.84-1.55 (m, 6H), 1.34-1.01 (m, 6H), 0.86-0.74 (m, 2H); <sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>)  $\delta$  198.6, 131.2, 130.0, 129.9, 129.6, 129.2, 128.8, 128.7, 128.4, 120.1, 116.7, 90.3, 51.7, 47.5, 42.0, 36.7, 33.8, 33.2, 33.1, 33.1, 26.5, 26.5, 26.3, 26.3; IR (film) 3237, 2925, 2852, 2209, 1727, 1628, 1449, 1358 cm<sup>-1</sup>; HRMS (FAB-MS)  $m/z$  196.0735 (196.0738 calc. for C<sub>11</sub>H<sub>11</sub>N<sub>1</sub>O<sub>1</sub>Na, M+Na<sup>+</sup>).

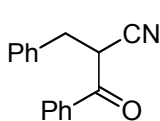
**3-Oxo-pentanenitrile (6aw).** Using general procedure A, acetonitrile (**4a**, 78.4 mg, 1.90 mmol) was converted into 179.8 mg (99%) of **6aw** as a colorless oil following column chromatography (SiO<sub>2</sub>, 20% EtOAc/Hexanes): *R<sub>f</sub>* = 0.17 (30% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>)  $\delta$  3.48 (s, 2H), 2.76 (q, *J* = 7.2 Hz, 2H), 1.14 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>)  $\delta$  198.5, 114.3, 36.0, 32.1, 7.8; IR (film) 2981, 2947, 2921, 2886, 2260, 1730, 1459, 1406, 1356, 1304 cm<sup>-1</sup>; HRMS no molecular ion found.

**3-Oxo-3-phenyl-propionitrile (6ax).** Using general procedure A, acetonitrile (**4a**, 78.4 mg, 1.90 mmol) was converted into 274.4 mg (99%) of **6ax** as a white solid following column chromatography (SiO<sub>2</sub>, 25% EtOAc/Hexanes): mp 81 °C; *R<sub>f</sub>* = 0.28 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>)  $\delta$  7.95-7.92 (m, 2H), 7.71-7.66 (m, 1H), 7.54-7.52 (m, 2H), 4.12 (s, 2H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>)  $\delta$  187.6, 135.2, 134.6, 129.5, 128.8, 29.8; IR (film) 3072, 2955, 2924, 2256, 1688, 1598, 1582, 1451, 1394, 1334, 1220, 1003 cm<sup>-1</sup>; HRMS (FAB-MS) *m/z* 168.0423 (168.0425 calc. for C<sub>9</sub>H<sub>7</sub>N<sub>1</sub>O<sub>1</sub>Na, M+Na<sup>+</sup>).

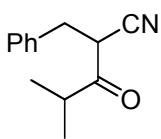
**4-Methyl-3-oxo-pentanenitrile (6ay).** Using general procedure A, acetonitrile (**4a**, 82 μL, 1.58 mmol) was converted into 146.2 mg (84%) of **6ay** as a colorless oil following column chromatography (SiO<sub>2</sub>, 25% EtOAc/Hexanes) (*Warning: product 6ay is extremely volatile!*): *R<sub>f</sub>* = 0.16 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>)  $\delta$  3.54 (s, 2H), 2.85-2.80 (m, 1H), 1.19 (d, *J* = 6.8 Hz, 6H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>)  $\delta$  114.3, 40.9, 30.5, 18.2; IR (film) 2977, 2262, 1725, 1468, 1388, 1305, 1046 cm<sup>-1</sup>; HRMS (GCMS) *m/z* 111.0680 (111.0684 calc. for C<sub>6</sub>H<sub>9</sub>N<sub>1</sub>O<sub>1</sub>, M<sup>+</sup>).

**4-Cyclohexyl-3-oxo-butyronitrile (6az).** Using general procedure A, acetonitrile (**4a**, 78.4 mg, 1.90 mmol) was converted into 302 mg (96%) of **6az** as a colorless oil following column chromatography (SiO<sub>2</sub>, 5% EtOAc/Hexanes): *R<sub>f</sub>* = 0.16 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>)  $\delta$  3.44 (s, 2H), 2.50 (d, *J* = 6.8 Hz, 2H), 1.90-1.85 (m, 1H), 1.70-1.65 (m, 5H), 1.35-1.14 (m, 3H), 1.02-0.93 (m, 2H); <sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>)  $\delta$  197.1, 113.8, 49.7, 33.7, 32.9, 32.5, 26.0, 25.9; IR (film) 2925, 2852, 2259, 1730, 1449, 1399, 1310 cm<sup>-1</sup>; HRMS (FAB-MS) *m/z* 188.1056 (188.1051 calc. for C<sub>10</sub>H<sub>15</sub>N<sub>1</sub>O<sub>1</sub>Na, M+Na<sup>+</sup>).

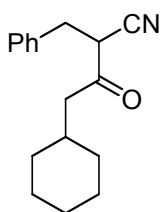
**2-Benzyl-3-oxo-pentanenitrile (6cw).** Using general procedure A, 3-phenyl-propionitrile (**4c**, 115.7 mg, 0.88 mmol) was converted into 148.1 mg (89%) of **6cw** as a colorless oil following column chromatography (SiO<sub>2</sub>, 10% EtOAc/Hexanes): *R<sub>f</sub>* = 0.42 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>)  $\delta$  7.39-7.24 (m, 5H), 3.66 (dd, *J* = 8.5 Hz, 5.6 Hz, 1H), 3.28-3.08 (m, 2H), 2.73-2.54 (m, 2H), 1.08 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>)  $\delta$  201.6, 136.0, 129.4, 129.3, 128.1, 117.7, 45.9, 35.8, 35.4, 7.8; IR (film) 2940, 2243, 1727, 1456 cm<sup>-1</sup>; HRMS (FAB-MS) *m/z* 210.0888 (210.0895 calc. for C<sub>12</sub>H<sub>13</sub>N<sub>1</sub>O<sub>1</sub>Na, M+Na<sup>+</sup>).



**2-Benzyl-3-oxo-3-phenyl-propionitrile (6cx).** Using general procedure A, 3-phenyl-propionitrile (**4c**, 118.2 mg, 0.90 mmol) was converted into 200.5 mg (95%) of **6cx** as a white solid following column chromatography (SiO<sub>2</sub>, 10% EtOAc/Hexanes): mp 85 °C; *R<sub>f</sub>* = 0.27 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>) \_ 7.99-7.29 (m, 10H), 4.54 (dd, *J* = 8.8 Hz, 5.8 Hz, 1H), 3.42-3.23 (m, 2H); <sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>) \_ 190.4, 136.4, 134.5, 129.5, 129.4, 129.3, 129.2, 128.0, 117.4, 88.5, 42.2, 35.9; IR (film) 3062, 3028, 2926, 2242, 1698, 1595, 1496, 1418, 1284, 1102 cm<sup>-1</sup>; HRMS (FAB<sup>+</sup>) *m/z* 258.0906 (258.0895 calc. for C<sub>16</sub>H<sub>13</sub>N<sub>1</sub>O<sub>1</sub>Na, M+Na<sup>+</sup>).

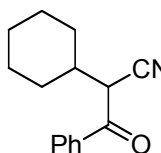


**2-Benzyl-4-methyl-3-oxo-pentanitrile (6cy).** Using general procedure A, 3-phenyl-propionitrile (**4c**, 124.6 mg, 0.95 mmol) was converted into 166.7 mg (89%) of **6cy** as a colorless oil: *R<sub>f</sub>* = 0.39 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>) \_ 7.39-7.25 (m, 5H), 3.78-3.73 (dd, *J* = 8.3 Hz, 6.0 Hz, 1H), 3.29-3.08 (m, 2H), 2.95-2.84 (m, 1H), 1.13 (dd, *J* = 6.8 Hz, 1.3 Hz, 6H); <sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>) \_ 204.4, 136.3, 129.4, 129.3, 117.6, 44.3, 40.6, 35.4, 18.4, 18.2; IR (film) 2976, 2244, 1726, 1460 cm<sup>-1</sup>; HRMS (ESI-MS) *m/z* 202.1225 (202.1232 calc. for C<sub>13</sub>H<sub>16</sub>N<sub>1</sub>O<sub>1</sub>, M+H<sup>+</sup>).



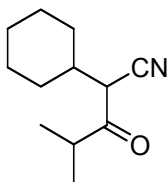
**2-Benzyl-4-cyclohexyl-3-oxo-butyronitrile (6cz).** Using general procedure A, 3-phenyl-propionitrile (**4c**, 165.8 mg, 1.26 mmol) was converted into 286.4 mg (88%) of **6cz** as a white solid following column chromatography (SiO<sub>2</sub>, 25% EtOAc/Hexanes): mp 62 °C; *R<sub>f</sub>* = 0.48 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>) \_ 7.39-7.26 (m, 5H), 3.62 (dd, *J* = 3.8 Hz, 2.5 Hz, 1H), 3.27-3.06 (m, 2H), 2.50 (d, *J* = 2.9 Hz, 2H), 1.92-1.83 (m, 1H), 1.80-1.60 (m, 5H), 1.34-1.07 (m, 3H), 0.97-0.86 (m, 2H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>) \_ 200.4, 136.1, 129.4, 129.3, 128.1, 117.7, 49.7, 46.5, 35.2, 33.7, 33.4, 33.3, 26.4, 26.4; IR (film) 2920, 2849, 2238, 1734, 1496, 1447, 1396 cm<sup>-1</sup>; HRMS (FAB-MS) *m/z* 278.1512 (278.1521 calc. for C<sub>17</sub>H<sub>21</sub>N<sub>1</sub>O<sub>1</sub>Na, M+Na<sup>+</sup>).

**2-Cyclohexyl-3-oxo-pentanitrile (6dw).** Using general procedure A, cyclohexylacetonitrile (**4d**, 203.6 mg, 1.66 mmol) was converted into 247.2 mg (83%) of **6dw** as a colorless oil following distillation at 120 °C at 200 mtorr: *R<sub>f</sub>* = 0.60 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>) \_ 3.31 (d, *J* = 5.6 Hz, 2H), 2.78-2.62 (m, 2H), 2.11-2.02 (m, 1H), 1.78-1.65 (m, 5H), 1.36-1.21 (m, 9H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>) \_ 210.8, 116.8, 52.3, 50.7, 38.2, 35.3, 31.3, 29.3, 25.8, 25.6, 25.4, 7.4; IR (film) 2980, 2931, 2856, 2246, 1726, 1451 cm<sup>-1</sup>; HRMS (FAB-MS) *m/z* 202.1218 (202.1208 calc. for C<sub>11</sub>H<sub>17</sub>N<sub>1</sub>O<sub>1</sub>Na, M+Na<sup>+</sup>).

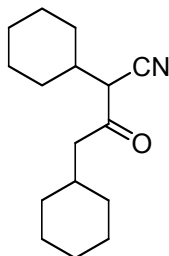


**2-Cyclohexyl-3-oxo-3-phenyl-propionitrile (6dx).** Using general procedure A, cyclohexylacetonitrile (**4d**, 158.6mg, 1.29 mmol) was converted into 260.2 mg (89%) of **6dx** as a colorless oil following column chromatography (SiO<sub>2</sub>, 10% EtOAc/Hexanes): *R<sub>f</sub>* = 0.35 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>) \_ 7.98-7.94 (m, 2H), 7.70-7.65 (m, 1H), 7.57-7.52 (m,

2H), 4.29 (d,  $J = 5.9$  Hz, 1H), 2.16-2.07 (m, 1H), 1.90-1.68 (m, 5H), 1.36-1.20 (m, 5H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ )  $\_$  191.4, 134.0, 134.8, 129.5, 129.1, 128.7, 116.9, 47.4, 39.3, 32.2, 29.8, 26.3, 26.0, 25.9; IR (film) 2930, 2855, 2246, 1690, 1596, 1449, 1344, 1291, 1250, 1228, 1212  $\text{cm}^{-1}$ ; HRMS (FAB-MS)  $m/z$  250.1205 (250.1208 calc. for  $\text{C}_{15}\text{H}_{17}\text{N}_1\text{O}_1\text{Na}$ ,  $\text{M}+\text{Na}^+$ ).



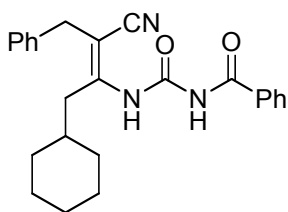
**2-Cyclohexyl-4-methyl-3-oxopentanenitrile (6dy).** Using general procedure A, cyclohexylacetonitrile (**4d**, 190.6 mg, 1.47 mmol) was converted into 275.0 mg (92%) of **6dy** as a colorless oil following column chromatography ( $\text{SiO}_2$ , 10% EtOAc/Hexanes):  $R_f = 0.48$  (25% EtOAc/Hexanes);  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ )  $\_$  3.42 (d,  $J = 5.7$  Hz, 1H), 3.03-2.96 (m, 1H), 2.13-2.06 (m, 1H), 1.82-1.65 (m, 4H), 1.39-1.12 (m, 12H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ )  $\_$  205.4, 117.2, 49.6, 40.4, 38.4, 31.8, 29.8, 26.3, 26.0, 25.9, 18.6, 18.5; IR (film) 2974, 2932, 2856, 2241, 1723, 1466, 1450  $\text{cm}^{-1}$ ; HRMS (FAB-MS)  $m/z$  216.1362 (216.1364 calc. for  $\text{C}_{12}\text{H}_{19}\text{N}_1\text{O}_1\text{Na}$ ,  $\text{M}+\text{Na}^+$ ).



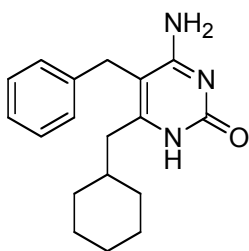
**2, 4-Dicyclohexyl-3-oxobutanenitrile (6dz).** Using general procedure A, cyclohexylacetonitrile (**4d**, 164.6 mg, 1.34 mmol) was converted into 296.0 mg (90%) of **6dz** as a colorless oil following distillation at 120 °C at 200 mtorr: mp 41 °C:  $R_f = 0.78$  (25% EtOAc/Hexanes);  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ )  $\_$  3.26 (d,  $J = 5.6$  Hz, 1H), 2.62-2.45 (m, 2H), 2.06-1.95 (m, 1H), 1.94-1.69 (m, 10H), 1.39-0.94 (m, 11H);  $^{13}\text{C}$  NMR (100MHz,  $\text{CDCl}_3$ )  $\_$  200.7, 116.8, 51.3, 49.3, 38.0, 33.3, 32.9, 31.4, 29.3, 26.0, 25.9, 25.8, 25.6, 25.5; IR (film) 2926, 2853, 2242, 1723, 1449  $\text{cm}^{-1}$ ; HRMS (FAB-MS)  $m/z$  270.1840 (270.1834 calc. for  $\text{C}_{16}\text{H}_{25}\text{N}_1\text{O}_1\text{Na}$ ,  $\text{M}+\text{Na}^+$ ).

**3-Amino-2-benzyl-4-cyclohexyl-but-2-enenitrile (7).** Ammonium formate (149.0 mg, 2.37 mmol) and molecular sieves (4Å, 251.0 mg) was added to a solution of 2-benzyl-4-cyclohexyl-3-oxo-butanenitrile (**6bz**, 119.6 mg, 0.47 mmol) in anhydrous ethyl alcohol (4 ml). The mixture was refluxed for 11 hours, and then diluted with brine (20 ml) and dichloromethane (40 ml). The organic layer was separated, washed with  $\text{H}_2\text{O}$  (40 ml  $\_$  2) and brine (40 ml  $\_$  2), dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated to afford light-yellow oil.

Column chromatography ( $\text{SiO}_2$ , 25% EtOAc/Hexanes) provided 110.7 mg (93%) of **7** as a colorless oil:  $R_f = 0.31$  (25% EtOAc/Hexanes);  $^1\text{H}$  NMR (300MHz,  $\text{CDCl}_3$ )  $\_$  7.36-7.23 (m, 5H), 4.18 (s, 1H), 3.45 (s, 2H), 2.36 (d,  $J = 7.3$  Hz, 2H), 1.78-1.59 (m, 6H), 1.31-0.95 (m, 5H);  $^{13}\text{C}$  NMR (75MHz,  $\text{CDCl}_3$ )  $\_$  159.2, 158.4, 138.5, 129.2, 128.9, 128.4, 128.3, 127.2, 126.9, 123.8, 42.6, 39.4, 37.6, 37.5, 33.9, 33.8, 33.6, 33.2, 26.6, 26.5; IR (film) 3474, 3356, 3249, 2924, 2851, 2182, 1637, 1597, 1449, 1382  $\text{cm}^{-1}$ ; HRMS (FAB-MS)  $m/z$  277.1677 (277.1681 calc. for  $\text{C}_{17}\text{H}_{22}\text{N}_2\text{Na}$ ,  $\text{M}+\text{Na}^+$ ).



**1-Benzoyl-3-(2-cyano-1-cyclohexylmethyl-3-phenyl-propenyl)-urea (9).** Benzoyl isocyanate (171.0 mg, 1.16 mmol) was added to a solution of 3-amino-2-benzyl-4-cyclohexyl-but-2-enenitrile (**7**, 74.0 mg, 0.29 mmol) and anhydrous pyridine (0.27 ml, 1.80 mmol) in anhydrous dichloromethane (2 ml). The mixture was stirred at R. T. for 10mins, and then diluted with brine (25 ml) and EtOAc (50 ml). The organic layer was separated, washed with H<sub>2</sub>O (50 ml  $\times$  2) and brine (50 ml  $\times$  2), dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated to afford a light-yellow solid. Column chromatography (SiO<sub>2</sub>, 25% EtOAc/hexanes) provided 107.7 mg (91%) of **9** as a white solid: mp 185 °C;  $R_f$  = 0.15 (25% EtOAc/Hexanes); <sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>) the major isomer  $\delta$  10.98 (s, 1H), 8.77 (s, 1H), 7.92-7.25 (m, 10H), 3.66 (s, 2H), 2.96 (d,  $J$  = 6.9 Hz, 2H), 1.73-1.57 (m, 6H), 1.24-1.07 (m, 5H); <sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>)  $\delta$  169.0, 150.8, 137.1, 134.4, 131.8, 129.5, 129.2, 128.9, 128.7, 128.2, 127.5, 120.1, 100.5, 40.8, 37.4, 35.0, 33.4, 33.0, 26.5; IR (film) 3261, 2928, 2853, 2207, 1703, 1621, 1543, 1501, 1470, 1265, 1228 cm<sup>-1</sup>; HRMS (FAB<sup>+</sup>)  $m/z$  424.2014 (424.2001 calc. for C<sub>25</sub>H<sub>27</sub>N<sub>3</sub>O<sub>2</sub>Na<sup>+</sup>, M+Na<sup>+</sup>).



**4-Amino-5-benzyl-6-cyclohexylmethyl-1H-pyrimidin-2-one (8).** Sodium hydride (25.0 mg, 0.64 mmol) was added to a solution of 1-benzoyl-3-(2-cyano-1-cyclohexyl-methyl-3-phenyl-propenyl)-urea (**9**, 65.5 mg, 0.16 mmol) in a mixture of anhydrous ethyl alcohol (3 ml) and benzene (2 ml). The mixture was refluxed for 11 hours, and then diluted with methyl alcohol (50 ml) and silica gel (10 mL). The mixture was concentrated and dry loaded onto a silica gel column. Column chromatography (SiO<sub>2</sub>, 50% EtOAc/hexanes  $\times$  20% MeOH/EtOAc) provided 38.5 mg (80%) of **8** as a white solid: mp 295 °C (decomposition observed);  $R_f$  = 0.35 (30% MeOH/EtOAc); <sup>1</sup>H NMR (300MHz, d<sub>6</sub>-DMSO)  $\delta$  10.36 (s, 1H), 7.38-6.50 (m, 7H), 3.70 (s, 2H), 2.24 (d,  $J$  = 7.0 Hz, 2H), 1.59-1.42 (m, 6H), 1.23-0.86 (m, 5H); <sup>13</sup>C NMR (75MHz, d<sub>6</sub>-DMSO)  $\delta$  167.3, 157.5, 154.3, 140.7, 129.9, 129.1, 128.5, 126.8, 100.7, 39.5, 37.7, 33.0, 30.0, 26.5; IR (film) 3429, 3106, 2922, 2849, 1679, 1657, 1624, 1480, 1445 cm<sup>-1</sup>; HRMS (FAB-MS)  $m/z$  320.1733 (320.1739 calc. for C<sub>18</sub>H<sub>23</sub>N<sub>3</sub>O<sub>2</sub>Na<sup>+</sup>, M+Na<sup>+</sup>).